REMARKS

Claims 1-3, 5-20 and 44-63 are now pending in this application. The Office Action rejects claims 1-20 and withdraws non-elected claims 21-43 from consideration. By this Amendment, the specification is amended; claims 1, 3, 5, 9 and 15-19 are amended; claims 4 and 21-43 are canceled; and claims 44-63 are added. In view of the amendments and the following remarks, reconsideration and allowance are respectfully requested.

I. Interview Summary

Applicants appreciate the courtesies shown to Applicants' representative by Examiner Davis in the February 12, 2004 personal interview. Applicants' separate record of the substance of the interview is incorporated into the following remarks, particularly in the discussion of Yland and of claim 3, which is similar to the proposed claim discussed during the interview.

II. Amendment of Specification

Applicants amend the specification to correct misspelling of the term "osmotic."

III. Rejections Under §112, Second Paragraph

The Office Action rejects claims 4, 5 and 9 under 35 U.S.C. §112, second paragraph. Applicants respectfully traverse the rejection.

The Office Action alleges that claim 4 is vague and indefinite, and that it is unclear how the scope of the claim is limited. The amendment cancels claim 4, rendering the rejection of this claim moot.

The Office Action alleges that in claim 5 the phrases "other recombinant tissue plasminogen activators" and "other mutant tPAs" renders claim 5 vague and indefinite. Amended claim 5, featuring a thrombolytic agent that may include "recombinant tissue plasminogen activator" and "mutant tissue plasminogen activator" satisfies the requirements of 35 U.S.C. §112, second paragraph.

The Office Action rejects claim 9, alleging that the phrase "or from about ten to about thirty or more units" renders claim 9 vague and indefinite. Amended claim 9 no longer recites this feature. Accordingly, claim 9 satisfies the requirements of 35 U.S.C. §112, second paragraph.

For at least these reasons, the claims clearly recite the invention. Therefore, the rejection under 35 U.S.C. §112, second paragraph, should be reconsidered and withdrawn.

IV. Rejections under §102

A. Yamauchi, Luh, Dubrul, Gundry and Pineo

The Office Action rejects claims 1, 4-6, 9 and 20 under 35 U.S.C. §102(a) over Yamauchi et al., Transplantation, 69: 1780 (2000) ("Yamauchi"); rejects claims 1, 4, 5, 9, 11 and 20 under 35 U.S.C. §102(a) over Luh et al., Transplantation 69: 2019 (2000) ("Luh"); rejects claims 1, 4-6 and 20 under 35 U.S.C. §102(b) over U.S. Patent No. 5,380,273 to Dubrul et al. ("Dubrul"); rejects claims 1, 4-10 and 20 under 35 U.S.C. §102(b) over Gundry et al., The Annals of Thoracic Surgery, 53: 772 (1992) ("Gundry"); and rejects claims 1, 4-10 and 17-20 under 35 U.S.C. §102(b) over Pineo et al., The Journal of Neurology, 138: 1223 (1987) ("Pineo"). Applicants respectfully traverse these rejections.

Claim 1 has been amended to recite that the organ is perfused *ex vivo* with a perfusion solution comprising a thrombolytic agent. None of Yamauchi, Luh, Dubrul, Gundry and Pineo teach perfusing an organ *ex vivo* with a perfusion solution comprising a thrombolytic agent. Although the Abstract of Gundry does not clearly indicate whether the heart is harvested before or after it is perfused with 250 mL of cold cardioplegia containing 200,000 units of streptokinase, a review of the entire article (copy attached) clearly indicates that the heart was harvested after this perfusion.

For at least this reason, Yamauchi, Luh, Dubrul, Gundry and Pineo do not teach each and every feature of claim 1. Claims 5-11 and 17-20 depend from claim 1. Therefore, the

rejections over Yamauchi, Luh, Dubrul, Gundry and Pineo should be reconsidered and withdrawn.

B. **Yland**

The Office Action rejects claims 1, 3, 4, 12 and 15-20 under 35 U.S.C. §102(b) over Yland et al., Transplantation International, 9: 535 (1996) ("Yland"). Applicants respectfully traverse this rejection.

Claims 1 and 3, which has been made independent herein, are both directed to a method of treating an organ that includes perfusing the organ with a solution comprising a thrombolytic agent. Yland does not teach such a method. Yland describes a perfusion system that utilizes heparinized solution. The Office Action takes the position that heparin is a thrombolytic agent. Applicants respectfully disagree.

A thrombolytic agent is an agent "that initiates dissolution of a blood clot." See the attached dictionary definition. In contrast, heparin is an organic compound that serves as an anticoagulant preventing the formation of blood clotting. However, heparin does not serve to dissolve blood clots. Thus, heparin is not a thrombolytic agent. Therefore, Yland does not teach the method of claims 1 or 3.

For at least this reason, Yland does not teach each and every feature of independent claims 1 and 3. Claims 4, 12 and 15-20 depend from either claim 1 or claim 3. Therefore, the rejection of these claims over Yland should be reconsidered and withdrawn.

V. **Rejections Under §103**

A. **Luh and Fahy**

The Office Action rejects claims 1-5 and 9-20 under 35 U.S.C. §103(a) over Luh in view of U.S. Patent No. 5,472,876 to Fahy ("Fahy"). Applicants respectfully traverse this rejection.

Independent claims 1 and 3 are both directed to a method of treating an organ with a thrombolytic agent to promote thrombolysis or prevent the formation of new thrombi. As discussed above, claim 1 has been amended to recite that the organ is perfused *ex vivo* with a perfusion solution comprising a thrombolytic agent. In contrast, Luh teaches flushing the organ with a solution containing urokinase *in vivo* through the left atrium. Luh does not teach or suggest perfusing an organ *ex vivo* with a perfusion solution comprising a thrombolytic agent, or that such a method can be used to promote thrombolysis or prevent the formation of new thrombi.

Claim 3 is directed to a method for treating an organ with a thrombolytic agent that includes connecting the organ to a perfusion circuit, perfusing the organ with a perfusion solution comprising a thrombolytic agent, measuring at least one parameter that indicates a level of thrombolysis, and determining whether thrombolysis occurs. As indicated in the Office Action, Luh does not teach a method that includes a perfusion circuit.

Neither Luh nor Fahy provides any motivation to use the apparatus described in Fahy in order to perfuse an organ with a perfusion solution comprising a thrombolytic agent. In particular, Fahy is directed to an apparatus and method for perfusing a organ, particularly with cryoprotectant agents. Fahy does not teach or suggest perfusing an organ with a perfusion solution comprising a thrombolytic agent.

In addition, Fahy does not overcome the deficiencies of Luh. In particular, Fahy does not teach or suggest perfusing an organ *ex vivo* with a perfusion solution comprising a thrombolytic agent, as recited in claim 1, or that such a method can be used to promote thrombolysis or prevent the formation of new thrombi. In addition, Fahy does not teach or suggest a method that includes "measuring at least one parameter that indicates a level of thrombolysis," or "determining whether thrombolysis occurs," as recited in claim 3.

For at least these reasons, Luh and Fahy fail to teach or suggest the methods of claims 1 and 3. Claims 2, 5 and 9-20 depend from either claim 1 or claim 3. Therefore, the rejection of these claims over Luh in view of Fahy should be reconsidered and withdrawn.

B. Dubrul

The Office Action rejects claims 1, 4-10 and 17-20 under 35 U.S.C. §103(a) over Dubrul. Applicants respectfully traverse the rejection.

As discussed above, claim 1 is directed to a method comprising perfusing an organ *ex vivo* with a perfusion solution comprising a thrombolytic agent. In contrast, Dubrul is directed to a catheter that can be placed in a blocked lumen in the body and may dispense a medicament suitable for dissolving the blockage. Dubrul does not teach or suggest a method comprising perfusing an organ *ex vivo* with a perfusion solution comprising a thrombolytic agent.

For at least this reason, Dubrul does not teach or suggest the method of claim 1. Claims 5-10 and 17-20 depend from claim 1. Therefore, the rejection of these claims over Dubrul should be reconsidered and withdrawn.

C. Yland

The Office Action rejects claims 1-4, 9, 10 and 12-20 under 35 U.S.C. §103(a) over Yland. Applicants respectfully traverse the rejection.

As detailed above, Yland describes a perfusion system that utilizes heparin. Yland does not teach or suggest a method that utilizes a thrombolytic agent, as recited in independent claims 1 and 3.

For at least this reason, Yland does not teach or suggest the method of claims 1 and 3. Claims 2, 9, 10 and 12-20 depend on either claim 1 or claim 3. Therefore, the rejection of these claims over Yland should be reconsidered and withdrawn.

D. **Yamauchi, Gundry, Pineo and Fahy**

The Office Action rejects claims 1-10 and 12-20 under 35 U.S.C. §103(a) over Yamauchi, Gundry or Pineo in view of Fahy. Applicants respectfully traverse this rejection.

As discussed above, independent claims 1 and 3 are both directed to a method of treating an organ with a thrombolytic agent to promote thrombolysis or prevent the formation of new thrombi. Claim 1 recites that the organ is perfused *ex vivo* with a perfusion solution comprising a thrombolytic agent. None of Yamauchi, Gundry or Pineo teach perfusing an organ *ex vivo* with a perfusion solution comprising a thrombolytic agent, or that such a method can be used to promote thrombolysis or prevent the formation of new thrombi.

Claim 3 is directed to a method for treating an organ with a thrombolytic agent that includes connecting the organ to a perfusion circuit, perfusing the organ with a perfusion solution comprising a thrombolytic agent, measuring at least one parameter that indicates a level of thrombolysis, and determining whether thrombolysis occurs. As indicated in the Office Action, none of Yamauchi, Gundry or Pineo teach a method that includes a perfusion circuit.

None of Yamauchi, Gundry, Pineo or Fahy provide any motivation to use the apparatus described in Fahy in order to perfuse an organ with a perfusion solution comprising a thrombolytic agent. As discussed above, Fahy is directed to an apparatus and method for perfusing a organ, particularly with cryoprotectant agents. Fahy does not teach or suggest perfusing an organ with a perfusion solution comprising a thrombolytic agent.

In addition, Fahy does not overcome the deficiencies of Yamauchi, Gundry or Pineo. In particular, Fahy does not teach or suggest perfusing an organ *ex vivo* with a perfusion solution comprising a thrombolytic agent, as recited in claim 1, or that such a method can be used to promote thrombolysis or prevent the formation of new thrombi. In addition, Fahy does not teach or suggest a method that includes "measuring at least one parameter that

indicates a level of thrombolysis," or "determining whether thrombolysis occurs," as recited in claim 3.

For at least these reasons, Yamauchi, Gundry or Pineo in view of Fahy each fail to teach or suggest the methods of claims 1 and 3. Claims 2, 5-10 and 12-20 depend from either claim 1 or claim 3. Therefore, the rejection of these claims over Yamauchi, Gundry or Pineo in view of Fahy should be reconsidered and withdrawn.

E. **Yamauchi, Gundry, Pineo, Luh and Fahy**

The Office Action rejects claims 1-20 under 35 U.S.C. §103(a) over Yamauchi, Gundry or Pineo in view of Luh and Fahy. Applicants respectfully traverse this rejection.

As detailed in the above remarks, Yamauchi, Gundry or Pineo in view of Fahy do not teach or suggest the invention of independent claims 1 and 3. In addition, Luh does not overcome the deficiencies of the other references. In particular, Luh does not provide any motivation to use the apparatus described in Fahy in order to perfuse an organ with a perfusion solution comprising a thrombolytic agent. In addition, Luh does not teach or suggest perfusing an organ *ex vivo* with a perfusion solution comprising a thrombolytic agent, as recited in claim 1, or that such a method can be used to promote thrombolysis or prevent the formation of new thrombi. In addition, Luh does not teach or suggest a method that includes "measuring at least one parameter that indicates a level of thrombolysis," or "determining whether thrombolysis occurs," as recited in claim 3.

For at least these reasons, Yamauchi, Gundry or Pineo in view of Luh and Fahy each fail to teach or suggest the methods of claims 1 and 3. Claims 2 and 5-20 depend from either claim 1 or claim 3. Therefore, the rejection of these claims over Yamauchi, Gundry or Pineo in view of Luh and Fahy should be reconsidered and withdrawn.

VI. New Claims

New claims 44-63 have been added to further define the invention. Claims 44-48 depend from claim 1 and are therefore patentable for at least the reasons discussed above with regard to claim 1. Claims 49-63 substantially correspond to claims 2, 5-11, 17-20, 44, 45 and 48, except that they depend from claim 3 rather than claim 1. Therefore, claims 49-63 are patentable for at least the reasons discussed above with regard to claim 3.

VII. Conclusion

In view of the foregoing, it is respectfully submitted that this application is in condition for allowance. Favorable reconsideration and prompt allowance of claims 1-3, 5-20 and 44-63 are earnestly solicited.

Should the Examiner believe that anything further would be desirable in order to place this application in even better condition for allowance, the Examiner is invited to contact the undersigned at the telephone number set forth below.

Respectfully submitted,

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Attachments:
Gundry Article
Dictionary Definition

WPB:MLM/hs

Date: February 19, 2004

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